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Time of Flight — Next-Generation PET Takes Flight

By Dan Harvey
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While PET use is certainly growing, the technology itself is also evolving. The 2006 Society of Nuclear Medicine (SNM) meeting highlighted developments in PET technology.

One of the more interesting stories to emerge from the meeting involved a look to the past as an older concept staged a reemergence. Philips Medical Systems introduced its Gemini TF system, utilizing time-of-flight (TOF) technology. GE Healthcare, with its Discovery ST Elite, gave attendees an introductory look at a redesigned PET/CT system that can perform respiratory gated studies. Siemens, with its new TruePoint PET/CT platform, showcased a system that provides an extended field of view. The new products represent a natural, ongoing evolution of these companies' PET/CT technology.

'80s Flashback

The coupling of TOF and PET goes back more than 20 years. Seminal techniques were developed in the 1980s and used primarily for research purposes. But further development was stymied by limitations in spatial resolution, sensitivity, and reconstruction, as well as the emergence of bismuth germinate (BGO) detectors.

"The big reason that TOF didn't take off at that time was because of those detectors," recalls Scott Schubert, sales and marketing manager of PET/CT for GE Healthcare, who was personally involved in TOF research during that period. The sensitivity of the BGO detectors, he says, dramatically improved the signal-to-noise ratio and made TOF appear unnecessary.

"TOF wasn't successful because baseline performance was inferior to that of BGO," he recalls. "TOF improvements didn't achieve the performance level that the BGO systems could deliver at that time."

However, relatively recent scintillator and computer advancements, as well as the ongoing development of PET itself, generated a renaissance of interest in TOF. As PET has evolved, new designs now feature scintillators that come with better timing resolution, an improvement that has made the integration of TOF information possible. Now it appears that TOF could provide improved image quality, count rates, and throughput—and potentially lead to the routine use of TOF PET as a clinical imaging technique. Philips has picked up the ball and run with it.

TOF Explained

TOF sounds like the kind of acronym you'd find on a transportation manifest, but it actually refers to a physics principle. To best understand it, you need to look at conventional PET imaging, which involves the injection of a decaying radioactive agent into a patient. As each nucleus decays, a positron is released that immediately collides with an electron, creating an annihilation that releases a pair of photons, or gamma rays.

"The principle of PET is that a positron, which is antimatter, meets an electron, which is matter. When antimatter meets matter, the result is electromagnetic energy. That energy is released in the form of these two photons," explains Chaitanya R. Divgi, MD, chief of nuclear medicine and clinical molecular imaging at the University of Pennsylvania (Penn) School of Medicine, an institution that helped foster TOF's renewed development and utilizes the Philip's Gemini TF system, the first commercially available TOF PET product.



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These two photons travel away from the collision point at 180° from each other. "In other words, they are released in the exact opposite directions," says Divgi. "They can be observed by two detectors placed in coincidence, on opposite sides of each other."

After detecting the photons, the PET scanner's computer uses that information to calculate where the radioactive agent is concentrated and produce an image localizing the affected area.

The photons themselves arrive at slightly different times depending on their origination. Traditionally, this time difference (also called timing resolution) has not been measured. However, TOF PET imaging enables time-difference measurement. "Time of flight determines the amount of time between the recording of one event by one of the detectors and the recording of the other event by the other detector," says Divgi. "Therefore, if an event occurs at the midpoint between these two detectors, the difference in time would be zero. If the event occurs closer to one detector, there will be a delay before the other detector sees it."

TOF makes it possible for point of origination of annihilation to be more accurately predicted, which leads to more accurate imaging. Improved event localization reduces noise in image data, resulting in higher image quality, shorter imaging times, and lower dose to the patient.

Product Introduction

First out of the gate with a commercially available TOF clinical solution, Philips introduced the Gemini at the European Congress of Radiology meeting in March before showcasing it at the 2006 SNM meeting. The Gemini TF is the first clinical machine that encompasses hybrid PET/CT combined with TOF technology. It enables identification of the aforementioned time difference, or timing resolution, to within one half-billionth of a second. Divgi says it can precisely locate occurring events, a capability that results in unrivaled image quality and points to far-ranging potential. "This has expanded our use of PET," he says about the installation at Penn. "As it provides better site localization of positron annihilation, it produces a higher-quality reconstructed image. Users are better able to quantify and detect lesions."

Divgi adds that Penn had a hand in Gemini's genesis. Joel Karp, PhD, a Penn physicist, along with research colleagues, contributed to the development of the technology. "Dr. Karp has worked on time of flight for more than a decade," Divgi says.

Penn has used Gemini TF for research purposes since November 2005. Now, it routinely uses the system in the clinical setting (units also have been recently installed at the Montefiore Medical Center in New York, University Hospitals of Cleveland, and in facilities in Europe and Japan). The system provides significantly reduced image noise and increased spatial resolution and sensitivity. Besides improved image quality and lesion detectability, benefits include increased patient throughput.

Divgi reports that imaging can be accomplished with standard parameters. "We perform scans just as we would with any other non-TOF machine," he says. "The only difference is we get much better images, with better contrast and better signal-to-noise ratio. This makes it much easier to see smaller lesions."

According to Philips, with the Gemini TF, image sensitivity is increased two times over conventional PET. For a whole-body PET scan, image acquisition is accomplished in less than 10 minutes. With the system's sophisticated detector crystals, pixels absorb photons emitted from clinically relevant sites in the patient and convert them into light. That light source can then be processed by a combination of conventional electronics and sophisticated software to create an image. The Gemini design also integrates Philips' OpenView gantry, which increases patient comfort.

In the clinical setting, clinicians at Penn have found that TOF is especially useful in examining overweight patients who have been traditionally difficult to image. Conventional PET scanners tend to be limited as far as image quality because the patients' size can increase attenuation and scatter effects. Clinicians typically try and compensate by increasing dose and acquisition time, but these strategies yield only limited improvement.

Improving Count Rates

Specific areas of improvement in heavier patients are the chest and waist. These are the largest parts of the body, and they are even larger in such patients. As oncological clinicians try and cover large portions of the body—sometimes even the entire body—improved count rates become a critical factor.

"When you do that much coverage, improved image quality and/or throughput is important,

and TOF can improve PET performance by enhancing count rates," says Jonathan Frey, director of product marketing, molecular imaging for Siemens.

Frey points out that Siemens helped pioneer TOF in the 1980s and is reconsidering it from a long-term perspective. "We definitely see TOF as something worth looking at," he says. For right now, Siemens' main focus is on increasing count rates, which the company feels is the most profound issue in nuclear medicine, says Frey. To that end, Siemens has introduced its TruePoint technology, which has an extended field of view and greater than 78% improvement in counts. Showcased at the SNM meeting, Siemens' TruePoint PET/CT platform adds 33% more axial volume coverage to its PET/CT scanners. In addition, it improves workflow by using fewer bed positions and increased speed.

With its enlarged PET field of view, Siemens believes its TruePoint PET/CT technology provides more precise and detailed images that enable physicians to pinpoint the tiniest lesions and arteries in detail. Further, it can reduce injected dose to patients by 50%.

GE Healthcare isn't completely sold on TOF because of system requirements.

"In an ideal situation, TOF can improve image quality and reduce acquisition time; and if you can do both, it can reduce the injected dose to patients," says Karthik Kuppusamy, general manager of molecular imaging for GE Healthcare. "But that is assuming that TOF is built on a PET/CT system that has the highest sensitivity. If you build TOF on the highest PET/CT systems in the market, then you could accomplish those things."

With its Discovery ST Elite PET/CT scanner, the company believes it has moved in a more effective direction. The core of the system is the Discovery Dimension Console, which is fully integrated to optimize PET/CT workflow.

"Dimension enables ViewPoint reconstruction and 4-D Imaging to improve image quality on all patients, no matter what their size," says Kuppusamy. "Because of the streamlined workflow, it reduces acquisition time and dose can be adjusted because of 2-D and 3-D acquisition capabilities."

He adds that ViewPoint can improve the image quality by a factor of more than 60% for all patient types on any conventional system on the market. Further, the 4-D Imaging can freeze motion, which TOF can't do. This enables the system to perform respiratory gated studies which, in turn, allows physicians to determine tumor size and location with greater precision, thus improving diagnosis. In conventional PET studies, a patient's respiration can distort the image. "The biggest challenge that clinicians face is the freezing of motion," says Kuppusamy. "During an exam, the lungs and the diaphragm move all of the time. TOF won't freeze that motion, whereas 4-D imaging will. At a result, it improves lesion detectability."

Adds Schubert: "We believe that enhancements like ViewPoint reconstruction are more significant because they provide image quality improvements across all patient sizes. TOF's principle benefits are only for the larger patients."

The new Elite system includes a highly sensitive PET BGO detector for higher photon stopping power and sensitivity. It shortens scan times as well as provides improved image quality in both 2-D and 3-D modes.

Implementation Considerations

Schubert says the "ultimate goal of enhancements in PET imaging is the improvement of image quality." The three advanced systems now offered by GE, Philips, and Siemens attempt to address that goal. Which system customers will choose will most likely depend on a number of factors. One of the major considerations involves costs, particularly as it relates to TOF, as Divgi says. "Implementation could be determined by economics," he says. "While it's true that the technology is superior to non-TOF systems for imaging larger patients, you must consider that 60% of patients imaged are not obese."

As such, it may be hard to justify the extra cost implementation would entail for a smaller imaging center or community hospital. Such facilities may find the price tag prohibitive. The cost of the Philips' Gemini system is estimated at \$2 million. For this reason and others, TOF will supplement, not supplant, its existing PET systems. "Philips will not discontinue selling its non-TOF systems," Divgi says.

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